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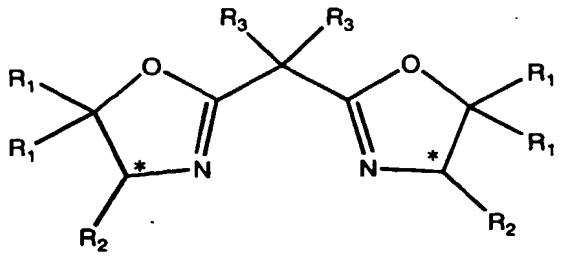
(54) Copper complexes of optically active bisoxazolines as enantioselective catalysts in cyclopropanation reactions

(57) An optically active bisoxazoline compound of the formula [I]:



[I]

wherein R_1 represents an alkyl group, cycloalkyl group, aralkyl group, phenyl group which may be substituted or an alkoxy group and two geminal alkyl groups may be joined together to form a cyclic structure;
R_2 represents an alkyl group , cycloalkyl group, aralkyl group or phenyl group which may be substituted;
R_3 represents a hydrogen atom, (C2-C4)alkyl group or cycloalkyl group; and
the asterisk * represents an asymmetric carbon atom.

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Description

[0001] The present invention relates to optically active bisoxazoline compounds, a process for producing them and a process for producing optically active cyclopropanecarboxylic acid derivatives using them.

[0002] The optically active cyclopropanecarboxylic acid esters are important compounds as intermediates for pharmaceuticals and pesticides. For example, (+)-2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropanecarboxylic acid, also known as chrysanthemum-monocarboxylic acid, constitutes the acid component of synthetic pyrethroid insecticides.

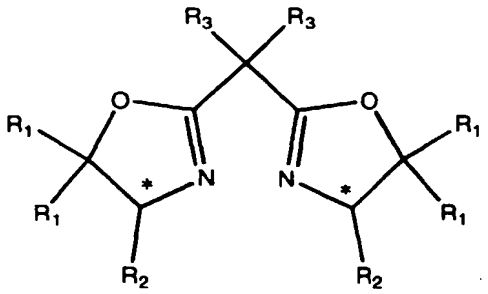
[0003] Conventionally, as the methods for directly producing optically active cyclopropanecarboxylic acid esters by synthetic technique, for example, a method has been known in which a prochiral olefin is reacted with a diazoacetic acid ester in the presence of an asymmetric copper complex using an optically active bis [2-(4,5-diphenyl-1,3-oxazolinyl)]methane as the ligand (Tetrahedron Lett., 32, 7373 (1991)).

[0004] Since, however, this method has problems that the raw material used for synthesizing the ligand is expensive and that the method for synthesizing the ligand is complicated, this method can not always be said to be an industrially advantageous method.

[0005] It is an object of the invention to provide optically active bisoxazoline compounds useful as asymmetric ligands for copper complexes which are used in preparing optically active cyclopropanecarboxylic acid esters by reacting an olefin with a diazoacetic acid ester.

[0006] The present invention provides:

1. an optically active bisoxazoline compound of the formula [I]:



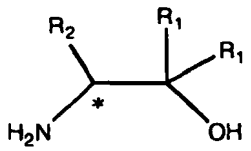
[I]

wherein R_1 represents an alkyl group, cycloalkyl group, aralkyl group, phenyl group which may be substituted, or an alkoxy group and the geminal alkyl groups may be joined together to form a cyclic structure;

R_2 represents an alkyl group, cycloalkyl group, aralkyl group, or phenyl group which may be substituted,

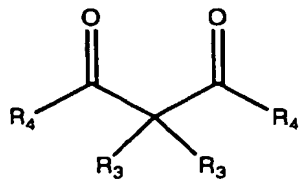
R_3 represents a hydrogen atom, (C2-C4)alkyl group or cycloalkyl group and the asterisk * represents an asymmetric carbon atom;

2. a process for producing the optically active bisoxazoline compound of the formula [I] which comprises reacting an optically active 2-amino alcohol of the formula [II]:



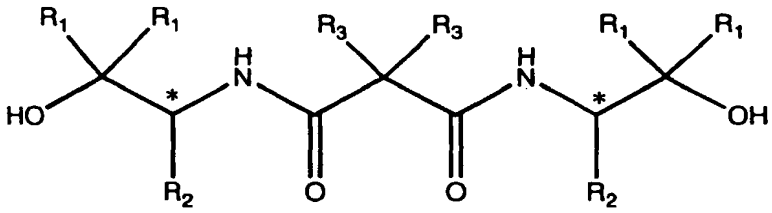
[II]

wherein R_1, R_2 and the asterisk * are as defined above, with a malonic acid derivative of the formula (3):



[III]

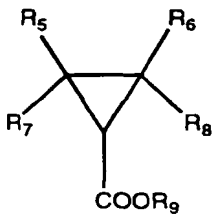
wherein R_3 is as defined above and R_4 represents an alkoxy group or halogen atom, to give a bisamido alcohol compound of the formula [IV]:



[IV]

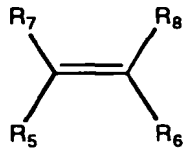
wherein R_1, R_2 and R_3 are as defined above,
and then subjecting the compound of the formula [IV] to a cyclization reaction in the presence of a Lewis acid catalyst; and

3. a process for producing an optically active cyclopropanecarboxylic acid derivative of the formula [VII] :



[VII]

wherein R_5, R_6, R_7 and R_8 are the same or different and represent a hydrogen atom, halogen atom, alkyl group, aralkyl group, aryl group, alkenyl group, alkyl group substituted with a halogen atom or an alkenyl group substituted with a halogen atom, with the proviso that when R_5 and R_6 represent the same group, then R_7 and R_8 represent different groups, and R_9 represents an alkyl group, cycloalkyl group or phenyl group which may be substituted, which comprises reacting a prochiral olefin of the formula [V]:



[V]

wherein R_5, R_6, R_7 and R_8 are as defined above, with a diazoacetic acid ester of the formula [VI]:

$$N_2CHCO_2R_9 \qquad [VI]$$

wherein R_9 is as defined above,

in the presence of a copper complex prepared from an optically active bisoxazoline compound of the formula [I] and a copper compound.

[0007] In the optically active bisoxazoline compounds [I] according to the present invention, the alkyl group represented by R_1 and R_2 includes e.g. a methyl group, ethyl group, n-propyl group, isopropyl group, n-butyl group, t-butyl group, n-amyl group, neopentyl group, n-hexyl group, n-octyl group and n-nonyl group, and the cycloalkyl group includes e.g. a cyclohexyl group and menthyl group.

[0008] Examples of the (C2-C4)alkyl group for R_3 include an ethyl, n-propyl group, n-butyl group and isobutyl group.

[0009] When R_1 is an alkyl group, two geminal alkyl groups may be joined together to form a cyclic structure containing 4 to 7 carbon atoms.

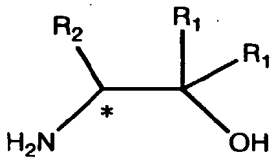
[0010] In the substituent R_1, the alkoxy group includes e.g. a methoxy group, ethoxy group, n-propoxy group and t-butoxy group. The aralkyl group includes e.g. a benzyl group, 2-phenylethyl group, 2-naphthylethyl group and diphenylmethyl group. The phenyl group which may be substituted includes e.g. a phenyl group, alkylphenyl group, alkoxyphenyl group and alkylalkoxyphenyl group.

[0011] These alkylphenyl, alkoxyphenyl, and alkylalkoxyphenyl groups include, for example a phenyl group substituted with 1 - 3 alkyl and/or alkoxy groups, respectively, described above at ortho-, meta- or para-position.

[0012] The optically active bisoxazoline compounds [I] according to the present invention have two asymmetric carbon atoms, as indicated by the asterisk *, and include at least two kinds of optical isomers resulting from the asymmetric carbon atoms. The optically active bisoxazoline compounds [I] according to the present invention comprise such optical isomers.

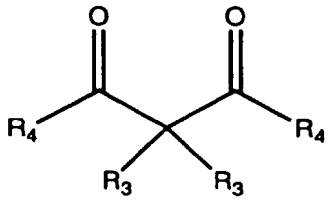
[0013] The optically active bisoxazoline compounds [I] according to the present invention are novel, and can be synthesized, for example, by the following process.

[0014] The optically active bisoxazoline compound [I] can be obtained by reacting an optically active 2-amino alcohol of the formula [II]:



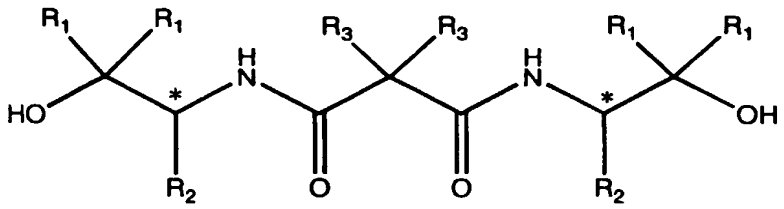
[II]

wherein R_1, R_2 and the asterisk * are as defined above, with a malonic acid derivative of the formula [III]:



[III]

wherein R_3 is as defined above and R_4 represents alkoxy group or halogen atom,
to give a bisamido alcohol compound of the formula [IV]:



[IV]

wherein R_1, R_2 and R_3 are as defined above,
and then subjecting this compound to cyclization in the presence of a Lewis acid catalyst.

[0015] The optically active 2-amino alcohol [II] includes:
for example,

(R)-2-amino-1,1-dimethylpropanol,

(R)-2-amino-1,1-diethylpropanol,

(R)-2-amino-1,1-di-n-propylpropanol,

(R)-2-amino-1,1-di-i-propylpropanol,

(R)-2-amino-1,1-dicyclohexylpropanol,

(R)-2-amino-1,1-dimethoxypropanol,

(R)-2-amino-1,1-diethoxypropanol,

(R)-2-amino-1,1-diphenylpropanol,

(R)-2-amino-1,1-di-(2-methylphenyl)propanol,

(R)-2-amino-1,1-di-(3-methylphenyl)propanol,

(R)-2-amino-1,1-di-(4-methylphenyl)propanol,

(R)-2-amino-1,1-di-(2-methoxyphenyl)propanol,

(R)-2-amino-1,1-di-(3-methoxyphenyl)propanol,

(R)-2-amino-1,1-di-(4-methoxyphenyl)propanol,

1-(1-(R)-aminoethyl)cyclobutanol,

1-(1-(R)-aminoethyl)cyclopentanol,

1-(1-(R)-aminoethyl)cyclohexanol,

1-(1-(R)-aminoethyl)cycloheptanol,

(R)-2-amino-3-methyl-1,1-dimethylbutanol,

(R)-2-amino-3-methyl-1,1-diethylbutanol,

(R)-2-amino-3-methyl-1,1-di-n-propylbutanol,

(R)-2-amino-3-methyl-1,1-di-i-propylbutanol,

(R)-2-amino-3-methyl-1,1-dicyclohexylbutanol,

(R)-2-amino-3-methyl-1,1-diphenylbutanol,

(R)-2-amino-3-methyl-1,1-di-(2-methylphenyl)butanol,

(R)-2-amino-3-methyl-1,1-di-(3-methylphenyl)butanol,

(R)-2-amino-3-methyl-1,1-di-(4-methylphenyl)butanol,

(R)-2-amino-3-methyl-1,1-di-(2-methoxyphenyl)butanol,

(R)-2-amino-3-methyl-1,1-di-(3-methoxyphenyl)butanol,

(R)-2-amino-3-methyl-1,1-di-(4-methoxyphenyl)butanol,

1-(1-(R)-amino-2-methyl-n-propyl)cyclobutanol,

1-(1-(R)-amino-2-methyl-n-propyl)cyclopentanol,

1-(1-(R)-amino-2-methyl-n-propyl)cyclohexanol,

1-(1-(R)-amino-2-methyl-n-propyl)cycloheptanol,

(R)-2-amino-4-methyl-1,1-dimethylpentanol,

(R)-2-amino-4-methyl-1,1-diethylpentanol,

(R)-2-amino-4-methyl-1,1-di-n-propylpentanol,

(R)-2-amino-4-methyl-1,1-di-i-propylpentanol,

(R)-2-amino-4-methyl-1,1-dicyclohexylpentanol,

(R)-2-amino-4-methyl-1,1-diphenylpentanol,

(R)-2-amino-4-methyl-1,1-di-(2-methylphenyl)pentanol,

(R)-2-amino-4-methyl-1,1-di-(3-methylphenyl)pentanol,

(R)-2-amino-4-methyl-1,1-di-(4-methylphenyl)pentanol,

(R)-2-amino-4-methyl-1,1-di-(2-methoxyphenyl)pentanol,

(R)-2-amino-4-methyl-1,1-di-(3-methoxyphenyl)pentanol,

(R)-2-amino-4-methyl-1,1-di-(4-methoxyphenyl)pentanol,

1-(1-(R)-amino-3-methyl-n-butyl)cyclobutanol,

1-(1-(R)-amino-3-methyl-n-butyl)cyclopentanol,

1-(1-(R)-amino-3-methyl-n-butyl)cyclohexanol,

1-(1-(R)-amino-3-methyl-n-butyl)cycloheptanol,

(R)-2-amino-3,3-dimethyl-1,1-dimethylbutanol,

(R)-2-amino-3,3-dimethyl-1,1-diethylbutanol,

(R)-2-amino-3,3-dimethyl-1,1-di-n-propylbutanol,

(R)-2-amino-3,3-dimethyl-1,1-di-i-propylbutanol,

(R)-2-amino-3,3-dimethyl-1,1-dicyclohexylbutanol,

(R)-2-amino-3,3-dimethyl-1,1-diphenylbutanol,

(R)-2-amino-3,3-dimethyl-1,1-di-(2methylphenyl)butanol,

(R)-2-amino-3,3-dimethyl-1,1-di-(3methylphenyl)butanol,

(R)-2-amino-3,3-dimethyl-1,1-di-(4methylphenyl)butanol,

(R)-2-amino-3,3-dimethyl-1,1-di-(2-methoxyphenyl)-butanol,

(R)-2-amino-3,3-dimethyl-1,1-di-(3-methoxyphenyl)-butanol,

(R)-2-amino-3,3-dimethyl-1,1-di-(4-methoxyphenyl)-butanol,

1-(1-(R)-amino-2,2-dimethyl-n-propyl)cyclobutanol,

1-(1-(R)-amino-2,2-dimethyl-n-propyl)cyclopentanol,

1-(1-(R)-amino-2,2-dimethyl-n-propyl)cyclohexanol,

1-(1-(R)-amino-2,2-dimethyl-n-propyl)cycloheptanol,

(R)-2-amino-2-phenyl-1,1-dimethylethanol,

(R)-2-amino-2-phenyl-1,1-diethylethanol,

(R)-2-amino-2-phenyl-1,1-di-n-propylethanol,

(R)-2-amino-2-phenyl-1,1-di-i-propylethanol,

(R)-2-amino-2-phenyl-1,1-dicyclohexylethanol,

(R)-2-amino-2-phenyl-1,1-diphenylethanol,

(R)-2-amino-2-phenyl-1,1-di-(2-methylphenyl)ethanol,

(R)-2-amino-2-phenyl-1,1-di-(3-methylphenyl)ethanol,

(R)-2-amino-2-phenyl-1,1-di-(4-methylphenyl)ethanol,

(R)-2-amino-2-phenyl-1,1-di-(2-methoxyphenyl)ethanol,

(R)-2-amino-2-phenyl-1,1-di-(3-methoxyphenyl)ethanol,

(R)-2-amino-2-phenyl-1,1-di-(4-methoxyphenyl)ethanol,

1-(1-(R)-aminophenylmethyl)cyclobutanol,

1-(1-(R)-aminophenylmethyl)cyclopentanol,

1-(1-(R)-aminophenylmethyl)cyclohexanol,

1-(1-(R)-aminophenylmethyl)cycloheptanol,

(R)-2-amino-2-benzyl-1,1-dimethylethanol,

(R)-2-amino-2-benzyl-1,1-diethylethanol,

(R)-2-amino-2-benzyl-1,1-di-n-propylethanol,

(R)-2-amino-2-benzyl-1,1-di-i-propylethanol,

(R)-2-amino-2-benzyl-1,1-dicyclohexylethanol,

(R)-2-amino-2-benzyl-1,1-diphenylethanol,

(R)-2-amino-2-benzyl-1,1-di-(2-methylphenyl)ethanol,

(R)-2-amino-2-benzyl-1,1-di-(3-methylphenyl)ethanol,

(R)-2-amino-2-benzyl-1,1-di-(4-methylphenyl)ethanol,

(R)-2-amino-2-benzyl-1,1-di-(2-methoxyphenyl)ethanol,

(R)-2-amino-2-benzyl-1,1-di-(3-methoxyphenyl)ethanol,

(R)-2-amino-2-benzyl-1,1-di-(4-methoxyphenyl)ethanol,

1-(1-(R)-amino-2-phenyl)cyclobutanol,

1-(1-(R)-amino-2-phenyl)cyclopentanol,

1-(1-(R)-amino-2-phenyl)cyclohexanol,

1-(1-(R)-amino-2-phenyl)cycloheptanol,

and

compounds having (S) configuration in the above compounds in place of (R), as well as salts of them such as e.g. hydrochloride, sulfate or acetate.

[0016] The optically active 2-amino alcohol [II] described above can readily be synthesized by reacting the corresponding optically active amino acid ester or its salt such as hydrochloride, sulfate or acetate with the corresponding Grignard reagent.

[0017] The optically active amino acid ester includes (R)-alanine methyl ester, (R)-valine methyl ester, (R)-leucine methyl ester, (R)-(t)-leucine methyl ester, (R)-phenylglycine methyl ester, (R)-phenylalanine methyl ester and compounds having a ethyl, propyl, n-butyl ester or other lower alkyl group in place of the methyl group in the above-described compounds.

[0018] Also usable are compounds having (S) configuration in the above-described compounds in place of (R), and salts of the above esters such as hydrochloride, sulfate or acetate.

[0019] The Grignard reagent includes:
methyl magnesium chloride, ethyl magnesium chloride, isopropyl magnesium chloride, n-propyl magnesium chloride, n-butyl magnesium chloride, cyclohexyl magnesium chloride, benzyl magnesium chloride, phenyl magnesium chloride, 2-methylphenyl magnesium chloride, 3-methylphenyl magnesium chloride, 4-methylphenyl magnesium chloride, 2-methoxyphenyl magnesium chloride, 3-methoxyphenyl magnesium chloride, 4-methoxyphenyl magnesium chloride, Grignard reagent obtained by reacting magnesium with 1,3-dichloropropane, 1,4-dichlorobutane, 1,5-dichloroheptane or 1,6-dichlorohexane and compounds having bromine atoms in the above compounds in place of chlorine atoms.

[0020] The malonic acid derivative of the formula [III] includes, for example, malonic acid diester compounds such as dimethyl malonate, diethyl malonate and diethyl diethylmalonate, and malonic acid halides such as malonyl dichloride, diethylmalonyl dichloride, malonyl dibromide and diethylmalonyl dibromide.

[0021] The amount to be used of such compounds is usually about 0.5 - 2 moles, preferably about 0.5 - 1 mole, per mol of the opticaly active 2-amino alcohol [II].

[0022] The Lewis acid includes, for example, titanium tetraisopropoxide, aluminumtriisopropoxide, dimethyltin dichloride, tin chloride and zinc chloride.
These Lewis acids, respectively, can be used independently or in combination of two or more.

[0023] The amount to be used of such compounds is usually about 0.001 - 5 moles, preferably about 0.01 - 1 mole, per mol of the opticaly active 2-amino alcohol [II].

[0024] In this the reaction, a solvent is usually used and such solvent includes, for example, toluene, xylene, heptane octane, chlorobenzene, methylene chloride and dichloroethylene.

[0025] These solvents, respectively, can be used independently or in combination of two or more.

[0026] The amount to be used of such compounds is not particularly limited but is usually about 2 - 200 parts by weight to 1 part by weight of the opticaly active 2-amino alcohol [II].

[0027] For the production of the optically active bisoxazoline compound [I] of the present invention, the bisamido alcohol [IV] is prepared according to the following process.

[0028] The optically active 2-amino alcohol [II] is usually reacted with the malonic acid diester in the above-described solvent. The reaction temperature is usually about 50 - 250°C, preferably about 60 - 180°C.

[0029] Alternatively, the optically active 2-amino alcohol [II] is usually reacted with the malonic acid dichloride in the presence of an appropriate base using the above-described solvent.

[0030] The base includes an organic base such as triethylamine, pyridine and 2,6-lutidine and an inorganic base such as potassium carbonate.
The amount of the base to be used is usually 2 moles or more per mol of the malonic acid dichloride. The reaction temperature is usually about -30 to 100°C, preferably about -10 to 50°C.

[0031] The obtained bisamido alcohol compound [IV] may either be isolated from the reaction mixture or used in the subsequent reaction step without isolation.

[0032] The production of the optically active bisoxazoline compound [I] from the bisamido alcohol compound [IV] can be performed by methods including a method in which either the above-described amount of the Lewis acid is added after dissolving the isolated bisamido alcohol compound [IV] in the above-described solvent or is added to the reaction solution containing the bisamido alcohol compound.

[0033] The reaction temperature is usually about 50 - 250°C, preferably about 60 - 180°C.

[0034] After the reaction is completed, the optically active bisoxazoline compound [I] corresponding to the optically active 2-amino alcohol [II] used can be obtained, for example, by adding an aqueous alkali solution such as an aqueous sodium hydrogen carbonate solution to the produced reaction mixture, filtering the precipitated solid off, concentrating the filtrate, adding water, extracting the produced solution with an organic solvent such as toluene, ethyl acetate or chloroform, and concentrating the obtained organic phase. The obtained optically active bisoxazoline compound [I] maybe purified by a conventional method, such as for example, distillation or column chromatography, Alternatively, after the reaction is completed, the reaction solution may be concentrated and directly subjected to post-treatment such as distillation or column chromatography to give the optically active bisoxazoline compound [I].

[0035] The steric configuration around the asymmetric carbon atom in the formula [I] representing the obtained optically active bisoxazoline compound is similar to that in the optically active form of the 2-amino alcohol [II] used.

[0036] The optically active bisoxazoline compound [I] includes:

methylenebis[(4R)-methyl-5,5-dimethyloxazoline],

methylenebis[(4R)-methyl-5,5-diethyloxazoline],

methylenebis[(4R)-methyl-5,5-di-n-propyloxazoline],

methylenebis[(4R)-methyl-5,5-di-i-propyloxazoline],

methylenebis[(4R)-methyl-5,5-dicyclohexyloxazoline],

methylenebis[(4R)-methyl-5,5-dimethoxyoxazoline],

methylenebis[(4R)-methyl-5,5-diethoxyoxazoline],

methylenebis[(4R)-methyl-5,5-diphenyloxazoline],

methylenebis[(4R)-methyl-5,5-di-(2-methylphenyl)-oxazoline],

methylenebis[(4R)-methyl-5,5-di-(3-methylphenyl)-

oxazoline],

methylenebis[(4R)-methyl-5,5-di-(4-methylphenyl)-oxazoline],

methylenebis[(4R)-methyl-5,5-di-(2-methoxyphenyl)-oxazoline],

methylenebis[(4R)-methyl-5,5-di-(3-methoxyphenyl)-oxazoline],

methylenebis[(4R)-methyl-5,5-di-(4-methoxyphenyl)-oxazoline],

methylenebis[spiro{(4R)-methyloxazoline-5,1'-cyclobutane}],

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2,2'-methylenebis[(4R)-i-propyl-5,5-diethyloxazoline],

2,2'-methylenebis[(4R)-i-propyl-5,5-di-n-propyl-oxazoline],

2,2'-methylenebis[(4R)-i-propyl-5,5-di-i-propyl-oxazoline],

2,2'-methylenebis[(4R)-i-propyl-5,5-dicyclohexyl-oxazoline],

2,2'-methylenebis[(4R)-i-propyl-5,5-diphenyloxazoline],
2,2'-methylenebis[(4R)-i-propyl-5,5-di-(2-methylphenyl)oxazoline],
2,2'-methylenebis[(4R)-i-propyl-5,5-di-(3-methylphenyl)oxazoline],
2,2'-methylenebis[(4R)-i-propyl-5,5-di-(4-methylphenyl)oxazoline],
2,2'-methylenebis[(4R)-i-propyl-5,5-di-(2-methoxyphenyl)oxazoline],
2,2'-methylenebis[(4R)-i-propyl-5,5-di-(3-methoxyphenyl)oxazoline],
2,2'-methylenebis[(4R)-i-propyl-5,5-di-(4-methoxyphenyl)oxazoline],
2,2'-methylenebis[spiro{(4R)-i-propyloxazoline-5,1'-cyclobutane}],
2,2'-methylenebis[spiro{(4R)-i-propyloxazoline-5,1'-cyclopentane}],
2,2'-methylenebis[spiro{(4R)-i-propyloxazoline-5,1'-cyclohexane}],
2,2'-methylenebis[spiro{(4R)-i-propyloxazoline-5,1'-cycloheptane}],
2,2'-methylenebis[(4R)-i-butyl-5,5-dimethyloxazoline],
2,2'-methylenebis[(4R)-i-butyl-5,5-diethyloxazoline],
2,2'-methylenebis[(4R)-i-butyl-5,5-di-n-propyloxazoline],

2,2'-methylenebis[(4R)-i-butyl-5,5-di-i-propyl-oxazoline],

2,2'-methylenebis[(4R)-i-butyl-5,5-dicyclohexyl-oxazoline],

2,2'-methylenebis[(4R)-i-butyl-5,5-diphenyloxazoline],

2,2'-methylenebis[(4R)-i-butyl-5,5-di-(2-methyl-phenyl)oxazoline],

2,2'-methylenebis[(4R)-i-butyl-5,5-di-(3-methyl-phenyl)oxazoline],

2,2'-methylenebis[(4R)-i-butyl-5,5-di-(4-methyl-phenyl)oxazoline],

2,2'-methylenebis[(4R)-i-butyl-5,5-di-(2-methoxy-phenyl)oxazoline],

2,2'-methylenebis[(4R)-i-butyl-5,5-di-(3-methoxy-phenyl)oxazoline],

2,2'-methylenebis[(4R)-i-butyl-5,5-di-(4-methoxy-phenyl)oxazoline],

2,2'-methylenebis[spiro{(4R)-i-butyloxazoline-5,1'-cyclobutane}],

2,2'-methylenebis[spiro{(4R)-i-butyloxazoline-5,1'-cyclopentane}],

2,2'-methylenebis[spiro{(4R)-i-butyloxazoline-5,1'-cyclohexane}],

2,2'-methylenebis[spiro{(4R)-i-butyloxazoline-5,1'-cycloheptane}],

2,2'-methylenebis[(4R)-t-butyl-5,5-dimethyloxazoline],

2,2'-methylenebis[(4R)-t-butyl-5,5-diethyloxazoline],

2,2'-methylenebis[(4R)-t-butyl-5,5-di-n-propyl-oxazoline],

2,2'-methylenebis[(4R)-t-butyl-5,5-di-i-propyl-oxazoline],

2,2'-methylenebis[(4R)-t-butyl-5,5-diphenyloxazoline],

2,2'-methylenebis[(4R)-t-butyl-5,5-dicyclohexyl-oxazoline],

2,2'-methylenebis[(4R)-t-butyl-5,5-di-(2-methyl-phenyl)oxazoline],

2,2'-methylenebis[(4R)-t-butyl-5,5-di-(3-methyl-phenyl)oxazoline],

2,2'-methylenebis[(4R)-t-butyl-5,5-di-(4-methyl-phenyl)oxazoline],

2,2'-methylenebis[(4R)-t-butyl-5,5-di-(2-methoxy-phenyl)oxazoline],

2,2'-methylenebis[(4R)-t-butyl-5,5-di-(3-methoxy-phenyl)oxazoline],

2,2'-methylenebis[(4R)-t-butyl-5,5-di-(4-methoxy-phenyl)oxazoline],

2,2'-methylenebis[spiro{(4R)-t-butyloxazoline-5,1'-cyclobutane}],

2,2'-methylenebis[spiro{(4R)-t-butyloxazoline-5,1'-cyclopentane}],

2,2'-methylenebis[spiro{(4R)-t-butyloxazoline-5,1'-cyclohexane}],

2,2'-methylenebis[spiro{(4R)-t-butyloxazoline-5,1'-cycloheptane}],

2,2'-methylenebis[(4R)-phenyl-5,5-dimethyloxazoline],

2,2'-methylenebis[(4R)-phenyl-5,5-diethyloxazoline],

2,2'-methylenebis[(4R)-phenyl-5,5-di-n-propyl-oxazoline],

2,2'-methylenebis[(4R)-phenyl-5,5-di-i-propyl-oxazoline],

2,2'-methylenebis[(4R)-phenyl-5,5-dicyclohexyl-oxazoline],

2,2'-methylenebis[(4R)-phenyl-5,5-diphenyloxazoline],

2,2'-methylenebis[(4R)-phenyl-5,5-di-(2-methylphenyl)-oxazoline],

2,2'-methylenebis[(4R)-phenyl-5,5-di-(3-methylphenyl)-oxazoline],

2,2'-methylenebis[(4R)-phenyl-5,5-di-(4-methylphenyl)-oxazoline],

2,2'-methylenebis[(4R)-phenyl-5,5-di-(2-methoxy-phenyl)oxazoline],

2,2'-methylenebis[(4R)-phenyl-5,5-di-(3-methoxy-phenyl)oxazoline],

2,2'-methylenebis[(4R)-phenyl-5,5-di-(4-methoxy-phenyl)oxazoline],

2,2'-methylenebis[spiro{(4R)-phenyloxazoline-5,1'-cyclobutane}],

2,2'-methylenebis[spiro{(4R)-phenyloxazoline-5,1'-cyclopentane}],

2,2'-methylenebis[spiro{(4R)-phenyloxazoline-5,1'-cyclohexane}],

2,2'-methylenebis[spiro{(4R)-phenyloxazoline-5,1'-cycloheptane}],

2,2'-methylenebis[(4R)-benzyl-5,5-dimethyloxazoline],

2,2'-methylenebis[(4R)-benzyl-5,5-diethyloxazoline],

2,2'-methylenebis[(4R)-benzyl-5,5-di-n-propyl-oxazoline],

2,2'-methylenebis[(4R)-benzyl-5,5-di-i-propyl-oxazoline],

2,2'-methylenebis[(4R)-benzyl-5,5-dicyclohexyl-oxazoline],

2,2'-methylenebis[(4R)-benzyl-5,5-diphenyloxazoline],

2,2'-methylenebis[(4R)-benzyl-5,5-di-(2-methylphenyl)-oxazoline],

2,2'-methylenebis[(4R)-benzyl-5,5-di-(3-methylphenyl)-oxazoline],

2,2'-methylenebis[(4R)-benzyl-5,5-di-(4-methylphenyl)-oxazoline],

2,2'-methylenebis[(4R)-benzyl-5,5-di-(2-methoxy-phenyl)oxazoline],

2,2'-methylenebis[(4R)-benzyl-5,5-di-(3-methoxyphenyl)oxazoline],

2,2'-methylenebis[(4R)-benzyl-5,5-di-(4-methoxyphenyl)oxazoline],

2,2'-methylenebis[spiro{(4R)-benzyloxazoline-5,1'-cyclobutane}],

2,2'-methylenebis[spiro{(4R)-benzyloxazoline-5,1'-cyclopentane}],

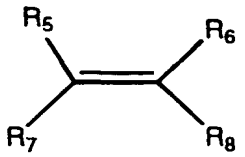
2,2'-methylenebis[spiro{(4R)-benzyloxazoline-5,1'-cyclohexane}],

2,2'-methylenebis[spiro{(4R)-benzyloxazoline-5,1'-cycloheptane}],

as well as compounds having (4S) configuration in the above compounds in place of (4R).

[0037] In addition, the bisoxazoline compounds include meso-form isomers having the (4R) configuration in the one oxazoline ring and having (4S) configuration in the other oxazoline ring in place of (4R) configuration in the above-described compounds.

[0038] The optically active cyclopropanecarboxylic acid derivative of the formula [VII] can be obtained in an industrially advantageous manner by reacting a prochiral olefin of the formula [V]:



[V]

wherein R_5, R_6, R_7 and R_8 are the same or different and represent a hydrogen atom, a halogen atom, an alkyl group, an aralkyl group, an aryl group, an alkenyl group, an alkyl group substituted with a halogen atom or atoms, or an alkenyl group substituted with a halogen atom or atoms, with the proviso that when R_5 and R_6 represent the same group, then R_7 and R_8 represent different groups,
with a diazoacetic acid ester of the formula [VI]:

$$N_2CHCO_2R_9 \qquad [VI]$$

wherein R_9 represents an alkyl group, cycloalkyl group or phenyl group which may be substituted,
in the presence of a copper complex prepared from an optically active bisoxazoline compound [I] produced as above and a copper compound.

[0039] The copper compound used for obtaining said copper complex includes, for example, a monovalent copper

compound such as copper (I) trifluoromethanesulfonate, $[Cu(CH_3CN)_4]PF_6$, $[Cu(CH_3CN)_4]ClO_4$, copper (I) acetate, copper (I) bromide and copper (I) chloride, and
divalent copper salts in which copper (I) moieties in the above compounds are replaced by copper (II). These can respectively be used independently or in combination of two or more. Preferably used is copper (II) trifluoromethanesulfonate and $[Cu(CH_3CN)_4]PF_6$, $[Cu(CH_3CN)_4]ClO_4$.

[0040] A solvent is usually used for the reaction of the above copper compound with the bisoxazoline ligand to obtain the copper complex, and such solvent includes, for example, halogenated hydrocarbons such as methylene chloride, 1,2-dichloroethane, chloroform and carbon tetrachloride and aromatic hydrocarbons such as benzene, toluene and xylene.

[0041] Alternatively, the prochiral olefin [V] to be used in the next step can be used in this step as a solvent.

[0042] The amount to be used of the solvent is usually about 50 - 500 parts by weight to 1 part by weight of the copper compound.

[0043] The amount to be used of the bisoxazoline compound [I] is usually about 0.8 - 5 moles, preferably about 1 - 2 moles per mol of the copper compound.

[0044] The reaction of the copper compound with the bisoxazoline compound [I] is usually carried out in an inert gas atmosphere such as argon or nitrogen.
From the viewpoint of the reaction yield, the above reaction is carried out in the absence of water.

[0045] The reaction temperature is not particularly limited and may usually be in a range of about 0 - 100°C.

[0046] In the present invention, when a divalent copper compound is used for preparing the complex, it is not necessary to reduce the copper compound to a monovalent counterpart using a reducing agent such as phenylhydrazine.

[0047] The copper complex obtained in this manner may be isolated or may be used as it is in the reaction of the prochiral olefin [V] and diazoacetic acid ester [VI] without isolation.

[0048] The amount to be used of the copper complex is usually about 0.0001 - 0.01 mol, preferably about 0.0002 - 0.002 mol, per mol of diazoacetic acid ester [VI], in terms of the copper compound.

[0049] Specific examples for the prochiral olefin of the formula [V] in the present invention include propene, 1-butene, isobutylene, 1-pentene, 1-hexene, 1-octene, 1-fluoro-1-chloroethene, 4-chloro-1-butene, 2-pentene, 2-heptene, 2-methyl-2-butene, 2,5-dimethyl-2,4-hexadiene, 2-methyl-2,4-hexadiene, 1-fluoro-1,1-dichloro-4-methyl-2-pentene, 2-chloro-5-methyl-2,4-hexadiene, 2-fluoro-5-methyl-2,4-hexadiene, 1,1,1-trifluoro-5-methyl-2,4-hexadiene, 2-methoxycarbonyl-5-methyl-2,4-hexadiene, 1,1-difluoro-4-methyl-1,3-pentadiene, 1,1-dichloro-4-methyl-1,3-pentadiene, 1,1-dibromo-4-methyl-1,3-pentadiene, 1-chloro-1-fluoro-4-methyl-1,3-pentadiene, 1-fluoro-1-bromo-4-methyl-1,3-pentadiene, 1,1,1-trichloro-4-methyl-3-pentene, 1,1,1-tribromo-4-methyl-3-pentene, 2,3-dimethyl-2-pentene, 2-methyl-3-phenyl-2-butene, 2-bromo-2,5-dimethyl-4-hexene, 2-chloro-2,5-dimethyl-4-hexene and 2,5-dimethyl-6-chloro-2,4-hexadiene, with 2,5-dimethyl-2,4-hexadiene being preferred.

[0050] Specific examples of R_9 in the diazoacetic acid [VI] used include a methyl, ethyl, propyl, isopropyl, butyl, isobutyl, s-butyl, t-butyl, n-pentyl, n-hexyl, l-menthyl, d-menthyl, benzyl, cyclohexyl, phenyl, m-methylphenyl, m-methoxyphenyl, 3,5-dimethylphenyl, 3,5-dimethoxyphenyl and 4-methyl-2,6-di-t-butylphenyl group.

[0051] Said diazoacetic acid esters [VI] can be obtained by known methods by subjecting, for example, the corresponding amino acid ester to the diazotization reaction and extracting the product with a halogenated hydrocarbon such as chloroform. The product can be isolated by distillation, if necessary.

[0052] The amount of the prochiral olefin [V] to be used in the above reaction is usually 2 moles or more, preferably 5 - 50 moles per mol of the diazoacetic acid ester [VI].

[0053] Specific methods for reacting the prochiral olefin [V] with the diazoacetic acid ester [VI] in the presence of the copper complex include, for example, the method wherein the diazoacetic acid ester [VI] dissolved in a solvent is added to a mixture of the copper complex as obtained in the manner described above and the prochiral olefin [V].

[0054] The solvent includes, for example, halogenated hydrocarbons such as dichloromethane, 1,2-dichloroethane, chloroform and carbon tetrachloride, aliphatic hydrocarbons such as hexane, heptane, cyclohexane, aromatic hydrocarbons such as benzene, toluene and xylene, and esters such as methyl acetate and ethyl acetate.

[0055] Alternatively, the prochiral olefin [V] can be used as the solvent. These can be used in combination.

[0056] The amount to be used of the solvent is usually 2 - 30 parts, preferably 5 - 20 parts by weight to 1 part by weight of the diazoacetic acid ester [VI].

[0057] The reaction of the prochiral olefin [V] with the diazoacetic acid ester [VI] is usually carried out in an inert gas atmosphere such as argon or nitrogen. From the viewpoint of the reaction yield, the above reaction is carried out in the absence of water.

[0058] The reaction temperature is not particularly limited and may be not more than the boiling point of the solvent, when used, or usually in a range of 0 - 100°C, preferably of 5 - 80°C.

[0059] The optically active cyclopropanecarboxylic acid esters [VII] obtained in the above reaction can be isolated, if necessary, by conventional methods such as distillation and column chromatography.

[0060] Specific compounds belonging to the optically active cyclopropanecarboxylic acid esters [VII] obtained in the

above reaction include, for example, optically active forms of:

2-fluoro-2-chlorocyclopropanecarboxylic acid ester,
2-methylcyclopropanecarboxylic acid ester,
2,2-dimethylcyclopropanecarboxylic acid ester,
2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropanecarboxylic acid ester,
2,2-dimethyl-3-(2,2-dichloro-1-ethenyl)cyclopropanecarboxylic acid ester,
2,2-dimethyl-3-(2,2,2-trichloroethyl)cyclopropanecarboxylic acid ester,
2,2-dimethylcy-3-(2,2,2-tribromoethyl)clopropanecarboxylic acid ester,
2,2-dimethyl-3-(2,2-dibromo-1-ethenyl)cyclopropanecarboxylic acid ester,
2,2-dimethyl-3-(2,2-difluoro-1-ethenyl)cyclopropanecarboxylic acid ester,

2,2-dimethyl-3-(2-fluoro-2-chloro-1-ethenyl)cyclopropanecarboxylic acid ester,

2,2-dimethyl-3-(2-fluoro-2-bromo-1-ethenyl)cyclopropanecarboxylic acid ester,

2,2-dimethyl-3-(2-fluoro-1-propenyl)cyclopropanecarboxylic acid ester,

2,2-dimethyl-3-(2-chloro-1-propenyl)cyclopropanecarboxylic acid ester,

2,2-dimethyl-3-(2-chloro-2,2,2-trifluoromethylethenyl)cyclopropanecarboxylic acid ester,

2,2-dimethyl-3-(2-methoxycarbonyl-1-propenyl)cyclopropanecarboxylic acid ester,

2,2-dimethyl-3-(2-chloro-2-methyl)propylcyclopropanecarboxylic acid ester,

2,2-dimethyl-3-(2-bromo-2-methyl)propylcyclopropanecarboxylic acid ester, and

2,2-dimethyl-3-(1-propenyl)cyclopropanecarboxylic acid ester.

[0061] The ester residue in the optically active cyclopropanecarboxylic acid esters [VII] includes, for example, a methyl, ethyl, n-propyl, i-propyl, i-butyl, t-butyl, cyclohexyl, menthyl and 4-methyl-2,6-di-t-butylphenyl group.

[0062] The optically active cyclopropanecarboxylic acid esters [VII] obtained in such manner can be converted into optically active cyclopropanecarboxylic acids having a hydrogen atom as the substituent R_9 by subjecting the ester to ester hydrolysis reaction according to the known methods.

[0063] In this reaction, the optically active cyclopropanecarboxylic acid esters [VII] produced according to the reaction of the present invention can be used for the ester hydrolysis reaction without isolation.

[0064] The methods for the above described ester hydrolysis reaction are not particularly limited and may be effected according to the known process including, for example, the hydrolysis using an alkali metal hydroxide, or the thermal decomposition by heating in the presence of an acid catalyst.

[0065] According to the present invention, the optically active cyclopropanecarboxylic acid esters [VII] can be produced in an industrially advantageous manner by reacting the prochiral olefin [V] and the diazoacetic acid ester [VI] in the presence of the copper complex prepared from a copper compound and the optically active bisoxazoline compound [I], which is the compound of the present invention and which can be synthesized from an optically active amino alcohol, which is synthesized from an optically active amino acid and a Grignard reagent.

EXAMPLES

[0066] The present invention will now be illustrated in more detail by reference of Examples, which should not be construed as a limitation upon the scope of the present invention.

Example 1

[0067] In an nitrogen atmosphere, 3.0 g (10.4 mmol) of (R)-2-amino-2-phenyl-1,1-diphenylethanol and 0.685 g (5.183 mmol) of dimethyl malonate were mixed with 150 ml of xylene and they were stirred at 120°C for 5 hours. Then, 147 mg (0.518 mmol) of titanium tetraisopropoxide was added to the reaction solution and the solution was stirred at 120°C for 48 hours.

[0068] After the reaction was completed, xylene was evaporated and the residue was purified by column chromatography (neutral alumina; ethyl acetate/hexane = 3/2) to give 2.35 g (yield: 74.1%) of 2,2'-methylenebis[(4R)-phenyl-5,5-diphenyloxazoline].

[0069] ^{1}HNMR ($CDCl_3$, TMS), δ : 3.91 (s, 2H); 6.82 - 7.14 (m, 18H); 7.33 - 7.43 (m, 8H); 7.68 (d, 4H).

Example 2

[0070] The procedure in Example 1 was repeated except that (R)-2-amino-2-phenyl-1,1-diphenylethanol was replaced by 2.66 g (10.4 mmol) of (S)-2-amino-3-methyl-1,1-diphenylbutanol to give 2.15 g of 2,2'-methylenebis[(4S)-i-propyl-5,5-diphenyloxazoline] (pale yellow powders, yield: 76.5%).

[0071] ^{1}HNMR ($CDCl_3$, TMS), δ : 0.64 (d, 6H, J = 6.9); 0.96 (d, 6H, J = 6.9); 1.70 - 1.85 (m, 2H); 3.64 (s, 2H); 4.63 (d, 2H, J = 4.9); 7.21 - 7.51 (m, 20H).

Example 3

[0072] The procedure in Example 1 was repeated except that (R)-2-amino-2-phenyl-1,1-diphenylethanol was replaced by 1.72 g (10.4 mmol) of (R)-2-amino-2-phenyl-1,1-dimethylethanol to give 1.42 g of 2,2'-methylenebis[(4R)-phenyl-5,5-dimethyloxazoline] (pale yellow oil, yield: 75.4%).

[0073] ^{1}HNMR ($CDCl_3$, TMS), δ : 0.88 (s, 6H); 1.60 (s, 6H); 3.53 (s, 2H); 4.90 (s, 2H); 7.20 - 7.35 (m, 10H).

Example 4

[0074] The procedure in Example 1 was repeated except that (R)-2-amino-2-phenyl-1,1-diphenylethanol was replaced by 1.99 g (10.4 mmol) of 1-((R)-minophenylmethyl)cyclopentanol to give 1.66 g of 2,2'-methylenebis[spiro{(4R)-phenyloxazoline-5,1'-cyclopentane}] (pale yellow oil, yield: 77.5%).

[0075] ^{1}HNMR ($CDCl_3$, TMS), δ : 1.00 - 1.83 (m, 16H); 3.55 (s, 2H); 5.01 (s, 2H); 7.20 - 7.34 (m, 10H).

Example 5: (Formation of cyclopropane ring)

[0076] In a 50 ml Schlenk's tube purged with nitrogen were placed 18.05 mg (0.05 mmol) of copper trifluoromethanesulfonate, 33.6 mg (0.055 mmol) of 2,2'-methylenebis[4(R)-phenyl-5,5-diphenyloxazoline] and 10 ml of n-butyl chloride, and the mixture was stirred at room temperature for 10 minutes. After adding 6.0 g (55 mmol) of 2,5-dimethyl-2,4-hexadiene, 1.1 g (10 mmol) of ethyl diazoacetate was added dropwise at 25°C over 2 hours. The stirring was continued at 25°C for 1 hour after the completion of the addition of ethyl diazoacetate. The amount of produced ethyl chrysanthemum-carboxylate was found 1.44 g as determined by gas chromatography. The yield based on ethyl diazoacetate was 73.6% and the trans/cis ratio was 72/28. After evaporating 2,5-dimethyl-2,4-hexadiene (boiling point: 51°C/30 mmHg), a 1g aliquot of the concentrated solution was taken out and subjected to alkaline hydrolysis by adding 10 ml of aqueous 1N sodium hydroxide solution and 5 ml of ethanol, and stirring at 100°C for 1 hour. The obtained chrysanthemum-carboxylic acid was reacted with 1-menthol and the produced diastereomeric esters were analyzed by gas chromatography. The optical purity of the trans-form was 64% e.e. and the optical purity of the cis-form was 35% e.e.

Example 6

[0077] The procedure in Example 5 was repeated except that 2,2'-methylenebis[4(R)-phenyl-5,5-diphenyloxazoline] was replaced by 29.8 mg (0.055 mmol) of 2,2-methylenebis[4(R)-i-propyl-5,5-diphenyloxazoline].
The obtained amount of ethyl chrysanthemum-carboxylate was 1.21 g, the yield was 61.6% and the trans/cis ratio was 64/36. The optical purity of the trans-form was 15% e.e. and the optical purity of the cis-form was 10% e.e.

Example 7

[0078] The procedure in Example 5 was repeated except that 2,2'-methylenebis[4(R)-phenyl-5,5-diphenyloxazoline] was replaced by 19.9 mg (0.055 mmol) of 2,2-methylenebis[4(R)-phenyl-5,5-dimethyloxazoline]. The obtained amount of ethyl chrysanthemum-carboxylate was 1.54 g, the yield was 78.6% and the trans/cis ratio was 74/26. The optical purity of the transform was 78% e.e. and the optical purity of the cis-form was 38% e.e.

Example 8

[0079] The procedure in Example 5 was repeated except that 2,2'-methylenebis[4(R)-phenyl-5,5-diphenyloxazoline] was replaced by 22.8 mg (0.055 mmol) of 2,2-methylenebis[spiro{4(R)-phenyloxazoline-5,1' cyclopentane}]. The obtained amount of ethyl chrysanthemum-carboxylate was 1.50 g, the yield was 76.3% and the trans/cis ratio was 74/26. The optical purity of the transform was 75% e.e. and the optical purity of the cis-form was 40% e.e.

Example 9

[0080] The procedure in Example 5 was repeated except that ethyl diazoacetate was replaced by 1.4 g (10 mmol) of t-butyl diazoacetate. The obtained amount of t-butyl chrysanthemum-carboxylate was 1.67 g, the yield was 74.4% and the trans/cis ratio was 79/21. Upon measurement by liquid chromatography, the optical purity of the trans-form was found 66% e.e. and the optical purity of the cis-form was found 45.2% e.e.

Example 10

[0081] The procedure in Example 9 was repeated except that 2,2'-methylenebis[4(R)-phenyl-5,5-diphenyloxazoline] was replaced by 19.9 mg (0.055 mmol) of 2,2-methylenebis[4(R)-phenyl-5,5-dimethyloxazoline]. The obtained amount of t-butyl chrysanthemum-carboxylate was 1.82 g, the yield was 81.2% and the trans/cis ratio was 85/15. The optical purity of the trans-form was 86% e.e. and the optical purity of the cis-form was 67% e.e.

Example 11

[0082] The procedure in Example 9 was repeated except that 2,2'-methylenebis[4(R)-phenyl-5,5-diphenyloxazoline] was replaced by 22.8 mg (0.055 mmol) of 2,2-methylenebis[spiro{4(R)-phenyloxazoline-5,1'-cyclopentane}]. The obtained amount of t-butyl chrysanthemum-carboxylate was 1.76 g, the yield was 78.6% and the trans/cis ratio was 84/16. The optical purity of the trans-form was 81% e.e. and the optical purity of the cis-form was 60% e.e.

Example 12

[0083] The procedure in Example 1 was repeated except that (R)-2-amino-2-phenyl-1,1-diphenylethanol was replaced by 5.19 g (17.9 mmol) of (R)-2-amino-2-phenyl-1,1-diethylethanol to give 1.33 g of 2,2'-methylenebis[(4R)-phenyl-5,5-diethyloxazoline] (pale yellow oil, yield: 38.4%).

[0084] ^{1}HNMR ($CDCl_3$, TMS), δ : 0.72 (t, 6H, J = 7.2); 1.04 (t, 6H, J = 7.2); 1.20 - 1.30 (m, 4H); 1.80-1.97 (m, 4H); 3.56 (s, 2H); 4.99 (s, 2H); 7.14 - 7.33 (m, 10H).

Example 13

[0085] The procedure in Example 1 was repeated except that (R)-2-amino-2-phenyl-1,1-diphenylethanol was replaced by 1.5 g (6.8 mmol) of (R)-2-amino-2-phenyl-1,1-di-n-propylethanol to give 1.08 g of 2,2'-methylenebis[(4R)-phenyl-5,5-di-n-propyloxazoline] (pale yellow powders, yield: 67.1%).

[0086] ^{1}HNMR ($CDCl_3$, TMS), δ : 0.61 (t, 6H, J = 6.9); 1.01 (t, 6H, J = 6.9); 0.97 - 1.61 (m, 16H); 3.55 (s, 2H); 4.97 (s, 2H); 7.14 - 7.35 (m, 10H).

Example 14

[0087] The procedure in Example 5 was repeated except that 2,2'-methylenebis[4(R)-phenyl-5,5-diphenyloxazoline] was replaced by 23.0 mg (0.055 mmol) of 2,2'-methylenebis[4(R)-pheny-5,5-diethylloxazoline]. The obtained amount of ethyl chrysanthemum-carboxylate was 1.59 g, the yield was 81.2% and the trans/cis ratio was 76/24. The optical purity of the trans-form was 76.3% e.e. and the optical purity of the cis-form was 45.9% e.e.

Example 15

[0088] The procedure in Example 5 was repeated except that 2,2'-methylenebis[4(R)-phenyl-5,5-diphenyloxazoline] was replaced by 26.5 mg (0.055 mmol) of 2,2'-methylenebis[4(R)-pheny-5,5-di-n-propyloxazoline]. The obtained amount of ethyl chrysanthemum-carboxylate was 1.03 g, the yield was 53.0% and the trans/cis ratio was 72/28. The optical purity of the trans-form was 71.4% e.e. and the optical purity of the cis-form was 38.5% e.e.

Example 16

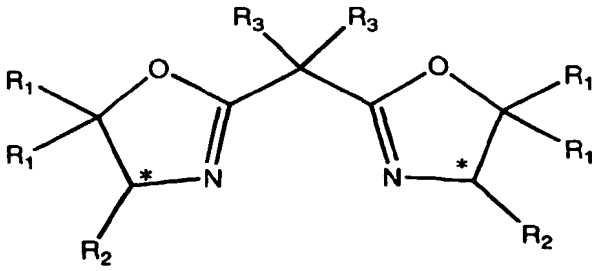
[0089] The procedure in Example 14 was repeated except that ethyl diazoacetate was replaced by 1.4g (10 mmol) of t-butyl diazoaxetate. The obtained amount of t-butyl chrysanthemum-carboxylate was 1.78 g, the yield was 79.6% and the trans/cis ratio was 84/16. The optical purity of the transform was 84.7% e.e. and the optical purity of the cis-form was 65.6% e.e.

Example 17

[0090] The procedure in Example 15 was repeated except that ethyl diazoacetate was replaced by 1.4g (10 mmol) of t-butyl diazoaxetate. The obtained amount of t-butyl chrysanthemum-carboxylate was 1.49 g, the yield was 66.5% and the trans/cis ratio was 83/17. The optical purity of the transform was 80.6% e.e. and the optical purity of the cis-form was 60.2% e.e.

Claims

1. An optically active bisoxazoline compound of the formula [I]:

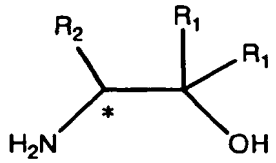


[I]

wherein R_1 represents an alkyl group, cycloalkyl group, aralkyl group, phenyl group which may be substituted, or an alkoxy group and two geminal alkyl groups may be joined together to form a cyclic structure;
R_2 represents an alkyl group, cycloalkyl group, aralkyl group, or phenyl group which may be substituted;
R_3 represents a hydrogen atom, (C2-C4)alkyl group or cycloalkyl group; and
the asterisk * represents an asymmetric carbon atom.

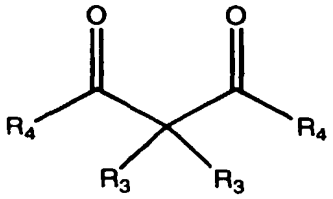
2. The optically active bisoxazoline compound according to claim 1, wherein R_2 in the formula [I] is a phenyl group which may be substituted.

3. A process for producing the optically active bisoxazoline compound of the formula [I] which comprises reacting an optically active 2-amino alcohol of the formula [II]:



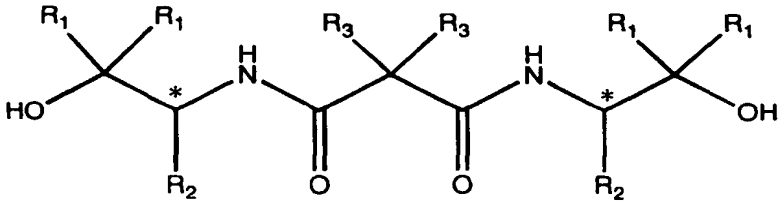
[II]

wherein R_1, R_2 and the asterisk * are as defined above, with a malonic acid derivative of the formula (3):



[III]

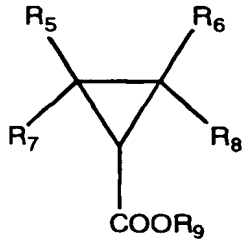
wherein R_3 is as defined above and R_4 represents an alkoxy group or halogen atom, to give a bisamido alcohol compound of the formula [IV]:



[IV]

wherein R_1, R_2 and R_3 are as defined above, and then subjecting the compound of the formula [IV] to cyclization in the presence of a Lewis acid catalyst.

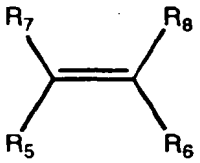
4. A process for producing an optically active cyclopropanecarboxylic acid derivative of the formula [VII]:



[VII]

wherein R_5, R_6, R_7 and R_8 are the same or different and represent a hydrogen atom, halogen atom, alkyl group, aralkyl group, aryl group, alkenyl group, alkyl group substituted with a halogen atom or an alkenyl group substituted with a halogen atom, with the proviso that when R_5 and R_6 represent the same group, then R_7 and R_8 represent different groups, and

R_9 represents an alkyl group, cycloalkyl group or phenyl group which may be substituted, which comprises reacting a prochiral olefin of the formula [V]:



[V]

wherein R_5, R_6, R_7 and R_8 are as defined above, with a diazoacetic acid ester of the formula [VI]:

$$N_2CHCO_2R_9 \qquad [VI]$$

wherein R_9 is as defined above,
in the presence of a copper complex prepared from an optically active bisoxazoline compound of the formula [I] and a copper compound.

5. The process according to claim 4, wherein the copper compound is copper (II) trifluoromethanesulfonate.

6. The process according to claim 4, wherein the prochiral olefin of the formula [VI is 2,5-dimethyl-2,4-hexadiene.

7. A bisamido alcohol compound of the formula [IV] as defined in claim 3.

8. A copper complex prepared from an optically active bisoxazoline compound of the formula [I] as defined in claim 1 and a copper compound.